

CLAIMS

We claim:

5 1. A method of treating neurodegeneration in a patient,
comprising

10 identifying a patient at risk for neurodegeneration; and
administering to the patient a therapeutically effective
amount of SUMOylation blocker.

15 2. The method of claim 1, wherein the SUMOylation blocker is
an inhibitor E1 SUMO activating enzyme.

3. The method of claim 1, wherein the SUMOylation blocker is
an inhibitor E2 SUMO conjugating enzyme.

20 4. The method of claim 1, wherein the SUMOylation blocker is
an inhibitor E3 SUMO ligating enzyme.

25 5. The method of claim 4, wherein the inhibitor of E3 SUMO
ligating enzyme is a PIAS protein.

6. A method of treating neurodegeneration in a patient,
comprising

30 identifying a patient at risk for neurodegeneration; and
administering to the patient a therapeutically effective
amount of deSUMOylation enhancer.

35 7. The method of claim 6, wherein the deSUMOylation enhancer
is SUMO isopeptidase.

8. A method of treating neurodegeneration in a patient,

1 52058/CAB/R2682

comprising

identifying a patient at risk for neurodegeneration; and
5 administering to the patient a therapeutically effective
amount of a Ubiquitination activator.

9. The method of claim 8, wherein the Ubiquitination
10 activator is an activator of E1 Ubiquitin activating enzyme.

10. The method of claim 8, wherein the Ubiquitination
activator is an activator of E1 Ubiquitin conjugating enzyme.

15 11. The method of claim 8, wherein the Ubiquitination
activator is an activator of E3 Ubiquitin ligating enzyme.

12. A method of treating neurodegeneration in a patient,
20 comprising

identifying a patient at risk for neurodegeneration; and
administering to the patient a therapeutically effective
amount of deUbiquitination inhibitor.

25 13. The method of claim 12, wherein the deUbiquitination
inhibitor is an inhibitor of Ubiquitin isopeptidase.

14. A method of treating polyglutamine-expansion-related
30 neurodegeneration in a patient, comprising

identifying a patient at risk for polyglutamine-
expansion-related neurodegeneration; and
administering to the patient a therapeutically effective
35 amount of SUMOylation blocker.

15. The method of claim 14, wherein the SUMOylation blocker

1 52058/CAB/R2682

is an inhibitor E1 SUMO activating enzyme.

5 16. The method of claim 14, wherein the SUMOylation blocker
is an inhibitor E2 SUMO conjugating enzyme.

10 17. The method of claim 14, wherein the SUMOylation blocker
is an inhibitor E3 SUMO ligating enzyme.

18. The method of claim 17, wherein the inhibitor of E3 SUMO
ligating enzyme is a PIAS protein.

15 19. A method of treating polyglutamine-expansion-related
neurodegeneration in a patient, comprising
identifying a patient at risk for polyglutamine-
expansion-related neurodegeneration; and
20 administering to the patient a therapeutically effective
amount of deSUMOylation enhancer.

25 20. The method of claim 19, wherein the deSUMOylation
enhancer is SUMO isopeptidase.

21. A method of treating polyglutamine-expansion-related
neurodegeneration in a patient, comprising
identifying a patient at risk for polyglutamine-
30 expansion-related neurodegeneration; and
administering to the patient a therapeutically effective
amount of a Ubiquitination activator.

35 22. The method of claim 21, wherein the Ubiquitination
activator is an activator of E1 Ubiquitin activating enzyme.

1 52058/CAB/R2682

23. The method of claim 21, wherein the Ubiquitination activator is an activator of E2 Ubiquitin conjugating enzyme.

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24. The method of claim 21, wherein the Ubiquitination activator is an activator of E3 Ubiquitin ligating enzyme.

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25. A method of treating polyglutamine-expansion-related neurodegeneration in a patient, comprising

identifying a patient at risk for polyglutamine-expansion-related neurodegeneration; and

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administering to the patient a therapeutically effective amount of deUbiquitination inhibitor.

26. The method of claim 25, wherein the deUbiquitination inhibitor is an inhibitor of Ubiquitin isopeptidase.

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27. A method of treating a neurodegenerative disease in a patient, comprising administering to the patient a therapeutically effective amount of SUMOylation blocker.

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28. The method of claim 27, wherein the SUMOylation blocker is an inhibitor E1 SUMO activating enzyme.

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29. The method of claim 27, wherein the SUMOylation blocker is an inhibitor E2 SUMO conjugating enzyme.

30. The method of claim 27, wherein the SUMOylation blocker is an inhibitor E3 SUMO ligating enzyme.

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31. The method of claim 30, wherein the inhibitor of E3 SUMO ligating enzyme is a PIAS protein.

1 52058/CAB/R2682

32. The method of claim 27, wherein the neurodegenerative
disease is one of more of the group consisting of Huntington's
5 disease, Alzheimer's disease, Parkinson's disease, amyotrophic
lateral sclerosis, Kennedy's disease, SCA1, DRPLA, epilepsy,
diabetes mellitus, spongiform encephalopathy, prion-related
disease, Machado-Joseph's disease and schizophrenia.

10 33. A method of treating a neurodegenerative disease in a
patient, comprising administering to the patient a
therapeutically effective amount of deSUMOylation enhancer.

15 34. The method of claim 33, wherein the deSUMOylation
enhancer is SUMO isopeptidase.

35. The method of claim 33, wherein the neurodegenerative
20 disease is one of more of the group consisting of Huntington's
disease, Alzheimer's disease, Parkinson's disease, amyotrophic
lateral sclerosis, Kennedy's disease, SCA1, DRPLA, epilepsy,
diabetes mellitus, spongiform encephalopathy, prion-related
disease, Machado-Joseph's disease and schizophrenia.

25 36. A method of treating a neurodegenerative disease in a
patient, comprising administering to the patient a
therapeutically effective amount of a Ubiquitination
30 activator.

37. The method of claim 36, wherein the Ubiquitination
activator is an activator of E1 Ubiquitin activating enzyme.

35 38. The method of claim 36, wherein the Ubiquitination
activator is an activator of E1 Ubiquitin conjugating enzyme.

39. The method of claim 36, wherein the Ubiquitination
5 activator is an activator of E3 Ubiquitin ligating enzyme.

40. A method of treating a neurodegenerative disease in a
patient, comprising administering to the patient a
10 therapeutically effective amount of a deUbiquitination
inhibitor.

41. The method of claim 40, wherein the deUbiquitination
15 inhibitor is an inhibitor of Ubiquitin isopeptidase.

42. The method of claim 40, wherein the neurodegenerative
disease is one of more of the group consisting of Huntington's
disease, Alzheimer's disease, Parkinson's disease, amyotrophic
20 lateral sclerosis, Kennedy's disease, SCA1, DRPLA, epilepsy,
diabetes mellitus, spongiform encephalopathy, prion-related
disease, Machado-Joseph's disease and schizophrenia.

43. A method of treating Huntington's disease in a patient,
25 comprising administering to the patient a therapeutically
effective amount of a SUMOylation blocker.

44. A method of treating Huntington's disease in a patient,
30 comprising administering to the patient a therapeutically
effective amount of a deSUMOylation enhancer.

45. A method of treating Huntington's disease in a patient,
35 comprising administering to the patient a therapeutically
effective amount of a Ubiquitination activator.

1 52058/CAB/R2682

46. A method of treating Huntington's disease in a patient,
comprising administering to the patient a therapeutically
5 effective amount of a deUbiquitination inhibitor.

47. A method of treating Kennedy's disease in a patient,
comprising administering to the patient a therapeutically
10 effective amount of a SUMOylation blocker.

48. A method of treating Kennedy's disease in a patient,
comprising administering to the patient a therapeutically
15 effective amount of a deSUMOylation enhancer.

49. A method of treating Kennedy's disease in a patient,
comprising administering to the patient a therapeutically
20 effective amount of a Ubiquitination activator.

50. A method of treating Kennedy's disease in a patient,
comprising administering to the patient a therapeutically
25 effective amount of a deUbiquitination inhibitor.

51. A method of treating spinocerebellar ataxia in a patient,
comprising administering to the patient a therapeutically
30 effective amount of a SUMOylation blocker.

52. A method of treating spinocerebellar ataxia in a patient,
comprising administering to the patient a therapeutically
35 effective amount of a deSUMOylation enhancer.

53. A method of treating spinocerebellar ataxia in a patient,
comprising administering to the patient a therapeutically
effective amount of a Ubiquitination activator.

54. A method of treating spinocerebellar ataxia in a patient,
5 comprising administering to the patient a therapeutically
effective amount of a deUbiquitination inhibitor.

55. A method of treating dentatorubral-pallidoluysian atrophy
10 in a patient, comprising administering to the patient a
therapeutically effective amount of a SUMOylation blocker.

56. A method of treating dentatorubral-pallidoluysian atrophy
15 in a patient, comprising administering to the patient a
therapeutically effective amount of a deSUMOylation enhancer.

57. A method of treating dentatorubral-pallidoluysian atrophy
in a patient, comprising administering to the patient a
20 therapeutically effective amount of a Ubiquitination
activator.

58. A method of treating dentatorubral-pallidoluysian atrophy
25 in a patient, comprising administering to the patient a
therapeutically effective amount of a deUbiquitination
inhibitor.

59. A method of treating protein-aggregation-related
30 neurodegeneration in a patient, comprising administering to
the patient a therapeutically effective amount of a
SUMOylation blocker.

60. A method of treating protein-aggregation-related
35 neurodegeneration in a patient, comprising administering to
the patient a therapeutically effective amount of a

1 52058/CAB/R2682

deSUMOylation enhancer.

5 61. A method of treating protein-aggregation-related neurodegeneration in a patient, comprising administering to the patient a therapeutically effective amount of a Ubiquitination activator.

10 62. A method of treating protein-aggregation-related neurodegeneration in a patient, comprising administering to the patient a therapeutically effective amount of a deUbiquitination inhibitor.

15 63. A method of treating Machado-Joseph's disease in a patient, comprising administering to the patient a therapeutically effective amount of a SUMOylation blocker.

20 64. A method of treating Machado-Joseph's disease in a patient, comprising administering to the patient a therapeutically effective amount of a deSUMOylation enhancer.

25 65. A method of treating Machado-Joseph's disease in a patient, comprising administering to the patient a therapeutically effective amount of a Ubiquitination activator.

30 66. A method of treating Machado-Joseph's disease in a patient, comprising administering to the patient a therapeutically effective amount of a deUbiquitination inhibitor.
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